PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and Administrative Instructions, Section 422)

To:

KEITH W NASH & CO
90-92 Regent Street
Cambridge CB2 1DP
ROYAUME-UNI

Date of mailing (day/month/year)
14 March 2000 (14.03.00)

Applicant's or agent's file reference
MTW50632/WO

IMPORTANT NOTIFICATION

International application No.
PCT/GB99/02165

International filing date (day/month/year)
06 July 1999 (06.07.99)

1. The following indications appeared on record concerning:

[ ] the applicant [ ] the inventor [X] the agent [ ] the common representative

Name and Address
HUMPHRIES, Martyn
ICI Group Intellectual Property
P.O. Box 90, Wilton
Middlesbrough
Cleveland TS90 8JE
United Kingdom

State of Nationality:
State of Residence:
Telephone No.: 01642 437419
Facsimile No.: 01642 436146
Teleprinter No.:

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[X] the person [ ] the name [ ] the address [ ] the nationality [ ] the residence

Name and Address
KEITH W NASH & CO
90-92 Regent Street
Cambridge CB2 1DP
United Kingdom

State of Nationality:
State of Residence:
Telephone No.: (01223) 355477
Facsimile No.: (01223) 324353
Teleprinter No.:

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

[X] the receiving Office
[ ] the International Searching Authority
[X] the International Preliminary Examining Authority
[ ] the designated Offices concerned
[X] the elected Offices concerned
[X] other: Former Agent HUMPHRIES, Martyn

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Facsimile No.: (41-22) 740.14.35

Authorized officer
Mougamadou ABIDINE
Telephone No.: (41-22) 338.83.38

Form PCT/IB/306 (March 1994)

003162647

MIL

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION CONCERNING SUBMISSION OR TRANSMITTAL OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

To:

HUMPHRIES, Martyn
ICI Group Intellectual Property
P.O. Box 90, Wilton
Middlesbrough
Cleveland TS90 8JE
ROYAUME-UNI

Date of mailing (day/month/year) 30 August 1999 (30.08.99)	
Applicant's or agent's file reference MTW50632/WO	**IMPORTANT NOTIFICATION**
International application No. PCT/GB99/02165	International filing date (day/month/year) 06 July 1999 (06.07.99)
International publication date (day/month/year) Not yet published	Priority date (day/month/year) 07 July 1998 (07.07.98)
Applicant QUEST INTERNATIONAL B.V. et al	

1. The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right-hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt, or by the letters "NR", in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).

2. This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.

3. An **asterisk(*)** appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b). In such a case, **the attention of the applicant is directed** to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

4. The **letters "NR"** appearing in the right-hand column denote a priority document which was not received by the International Bureau or which the applicant did not request the receiving Office to prepare and transmit to the International Bureau, as provided by Rule 17.1(a) or (b), respectively. In such a case, **the attention of the applicant is directed** to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

Priority date	Priority application No.	Country or regional Office or PCT receiving Office	Date of receipt of priority document
07 July 1998 (07.07.98)	9814653.3	GB	03 Augu 1999 (03.08.99)

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 740.14.35

Authorized officer

Juan Cruz

Telephone No. (41-22) 338.83.38

002817238

PCT

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

PCT receiving Office use only

International Application No.

International Filing Date

Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference *(if desired) (12 characters maximum)* MTW50632/WO

Box No. I TITLE OF INVENTION

METHOD OF REDUCING OR PREVENTING MALODOUR

Box No. II APPLICANT

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

QUEST INTERNATIONAL B.V.
Huizerstraatweg 28
1411 GP Naarden
Netherlands

☐ This person is also inventor.

Telephone No. 01642 437419

Facsimile No. 01642 436146

Teleprinter No. 94028500 ICIC G

State *(that is, country)* of nationality: NL

State *(that is, country)* of residence: NL

This person is applicant for the purposes of: ☐ all designated States ☒ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

WILSON, Craig Stewart
30 Tilden Close
High Halden
Kent TN26 3LR
UNITED KINGDOM

This person is:

☐ applicant only

☒ applicant and inventor

☐ inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality: GB

State *(that is, country)* of residence: GB

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

☒ Further applicants and/or (further) inventors are indicated on a continuation sheet.

Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as: ☒ agent ☐ common representative

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

HUMPHRIES, Martyn
ICI Group Intellectual Property
PO Box 90, Wilton, Middlesbrough
Cleveland, England TS90 8JE

Telephone No. 01642 437419

Facsimile No. 01642 436146

Teleprinter No. 94028500 ICIC G

☐ **Address for correspondence:** Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

Continuation of Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

If none of the following sub-boxes is used, this sheet should not be included in the request.

Name and address: *(Family name followed by given name: for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

MINHAS, Tony
30 King Edward Avenue
Dartford
Kent DA1 2HZ
UNITED KINGDOM

This person is:
- [ ] applicant only
- [X] applicant and inventor
- [ ] inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality: GB

State *(that is, country)* of residence: GB

This person is applicant for the purposes of:
- [ ] all designated States
- [ ] all designated States except the United States of America
- [X] the United States of America only
- [ ] the States indicated in the Supplemental Box

Name and address: *(Family name followed by given name: for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

BEHAN, JOHN MARTIN
The Forge
The Green
Boughton Aluph
Ashford
Kent TN25 4JB
UNITED KINGDOM

This person is:
- [ ] applicant only
- [X] applicant and inventor
- [ ] inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality: GB

State *(that is, country)* of residence: GB

This person is applicant for the purposes of:
- [ ] all designated States
- [ ] all designated States except the United States of America
- [X] the United States of America only
- [ ] the States indicated in the Supplemental Box

Name and address: *(Family name followed by given name: for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

This person is:
- [ ] applicant only
- [ ] applicant and inventor
- [ ] inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality:

State *(that is, country)* of residence:

This person is applicant for the purposes of:
- [ ] all designated States
- [ ] all designated States except the United States of America
- [ ] the United States of America only
- [ ] the States indicated in the Supplemental Box

Name and address: *(Family name followed by given name: for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

This person is:
- [ ] applicant only
- [ ] applicant and inventor
- [ ] inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality:

State *(that is, country)* of residence:

This person is applicant for the purposes of:
- [ ] all designated States
- [ ] all designated States except the United States of America
- [ ] the United States of America only
- [ ] the States indicated in the Supplemental Box

- [ ] Further applicants and/or (further) inventors are indicated on another continuation sheet.

Box No.V **DESIGNATION OF STATES**

The following designations are hereby made under Rule 4.9(a) *(mark the applicable check-boxes; at least one must be marked)*:

Regional Patent

- ☒ AP **ARIPO Patent:** **GH** Ghana, **GM** Gambia, **KE** Kenya, **LS** Lesotho, **MW** Malawi, **SD** Sudan, **SZ** Swaziland, **UG** Uganda, **ZW** Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT
- ☒ EA **Eurasian Patent:** **AM** Armenia, **AZ** Azerbaijan, **BY** Belarus, **KG** Kyrgyzstan, **KZ** Kazakhstan, **MD** Republic of Moldova, **RU** Russian Federation, **TJ** Tajikistan, **TM** Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT
- ☒ EP **European Patent:** **AT** Austria, **BE** Belgium, **CH** and **LI** Switzerland and Liechtenstein, **CY** Cyprus, **DE** Germany, **DK** Denmark, **ES** Spain, **FI** Finland, **FR** France, **GB** United Kingdom, **GR** Greece, **IE** Ireland, **IT** Italy, **LU** Luxembourg, **MC** Monaco, **NL** Netherlands, **PT** Portugal, **SE** Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT
- ☒ OA **OAPI Patent:** **BF** Burkina Faso, **BJ** Benin, **CF** Central African Republic, **CG** Congo, **CI** Côte d'Ivoire, **CM** Cameroon, **GA** Gabon, **GN** Guinea, **GW** Guinea-Bissau, **ML** Mali, **MR** Mauritania, **NE** Niger, **SN** Senegal, **TD** Chad, **TG** Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT *(if other kind of protection or treatment desired, specify on dotted line)* .....

National Patent *(if other kind of protection or treatment desired, specify on dotted line)*:

- ☒ AL Albania .....
- ☒ AM Armenia .....
- ☒ AT Austria .....
- ☒ AU Australia .....
- ☒ AZ Azerbaijan
- ☒ BA Bosnia and Herzegovina .....
- ☒ BB Barbados
- ☒ BG Bulgaria .....
- ☒ BR Brazil .....
- ☒ BY Belarus .....
- ☒ CA Canada
- ☒ CH and LI Switzerland and Liechtenstein
- ☒ CN China .....
- ☒ CU Cuba .....
- ☒ CZ Czech Republic .....
- ☒ DE Germany .....
- ☒ DK Denmark .....
- ☒ EE Estonia .....
- ☒ ES Spain .....
- ☒ FI Finland .....
- ☒ GB United Kingdom
- ☒ GD Grenada
- ☒ GE Georgia .....
- ☒ GH Ghana .....
- ☒ GM Gambia
- ☒ HR Croatia .....
- ☒ HU Hungary .....
- ☒ ID Indonesia
- ☒ IL Israel .....
- ☒ IN India .....
- ☒ IS Iceland
- ☒ JP Japan .....
- ☒ KE Kenya .....
- ☒ KG Kyrgyzstan .....
- ☒ KP Democratic People's Republic of Korea .....
- ☒ KR Republic of Korea .....
- ☒ KZ Kazakhstan .....
- ☒ LC Saint Lucia
- ☒ LK Sri Lanka
- ☒ LR Liberia
- ☒ LS Lesotho .....
- ☒ LT Lithuania
- ☒ LU Luxembourg
- ☒ LV Latvia
- ☒ MD Republic of Moldova .....
- ☒ MG Madagascar .....
- ☒ MK The former Yugoslav Republic of Macedonia .....
- ☒ MN Mongolia
- ☒ MW Malawi .....
- ☒ MX Mexico .....
- ☒ NO Norway
- ☒ NZ New Zealand .....
- ☒ PL Poland .....
- ☒ PT Portugal .....
- ☒ RO Romania
- ☒ RU Russian Federation .....
- ☒ SD Sudan
- ☒ SE Sweden
- ☒ SG Singapore
- ☒ SI Slovenia .....
- ☒ SK Slovakia .....
- ☒ SL Sierra Leone
- ☒ TJ Tajikistan .....
- ☒ TM Turkmenistan .....
- ☒ TR Turkey .....
- ☒ TT Trinidad and Tobago .....
- ☒ UA Ukraine .....
- ☒ UG Uganda .....
- ☒ US United States of America .....
- ☒ UZ Uzbekistan .....
- ☒ VN Viet Nam .....
- ☒ YU Yugoslavia .....
- ☒ ZW Zimbabwe .....

Check-boxes reserved for designating States (for the purposes of a national patent) which have become party to the PCT after issuance of this sheet:

- ☒ SOUTH AFRICA .....
- ☐ .....
- ☐ .....

Precautionary Designation Statement: In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. *(Confirmation of a designation consists of the filing of a notice specifying that designation and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit.)*

Supplemental Box *If the Supplemental Box is not used, this sheet should not be included in the request.*

*1. If, in any of the Boxes, **the space is insufficient** to furnish all the information: in such case, write "Continuation of Box No. ..." [indicate the number of the Box] and furnish the information in the same manner as required according to the captions of the Box in which the space was insufficient, in particular:*

*(i) **if more than two persons are involved as applicants and/or inventors** and no "continuation sheet" is available: in such case, write "Continuation of Box No. III" and indicate for each additional person the same type of information as required in Box No. III. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below;*

*(ii) if, in Box No. II or in any of the sub-boxes of Box No. III, the indication **"the States indicated in the Supplemental Box"** is checked: in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the applicant(s) involved and, next to (each) such name, the State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is applicant;*

*(iii) if, in Box No. II or in any of the sub-boxes of Box No. III, the inventor or the inventor/applicant is **not inventor for the purposes of all designated States or for the purposes of the United States of America**: in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the inventor(s) and, next to (each) such name, the State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is inventor;*

*(iv) if, in addition to the agent(s) indicated in Box No. IV, there are **further agents**: in such case, write "Continuation of Box No. IV" and indicate for each further agent the same type of information as required in Box No. IV;*

*(v) if, in Box No. V, the name of any State (or OAPI) is accompanied by the indication **"patent of addition,"** or **"certificate of addition,"** or if, in Box No. V, the name of the United States of America is accompanied by an indication **"continuation"** or **"continuation-in-part"**: in such case, write "Continuation of Box No. V" and the name of each State involved (or OAPI), and after the name of each such State (or OAPI), the number of the parent title or parent application and the date of grant of the parent title or filing of the parent application;*

*(vi) if, in Box No. VI, there are **more than three earlier applications whose priority is claimed**: in such case, write "Continuation of Box No. VI" and indicate for each additional earlier application the same type of information as required in Box No. VI;*

*(vii) if, in Box No. VI, **the earlier application is an ARIPO application**: in such case, write "Continuation of Box No. VI", specify the number of the item corresponding to that earlier application and indicate at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed.*

*2. If, with regard to the **precautionary designation statement** contained in Box No. V, the applicant wishes to exclude any State(s) from the scope of that statement: in such case, write "Designation(s) excluded from precautionary designation statement" and indicate the name or two-letter code of each State so excluded.*

*3. If the applicant claims, in respect of any designated Office, the benefits of provisions of the national law concerning **non-prejudicial disclosures or exceptions to lack of novelty**: in such case, write "Statement concerning non-prejudicial disclosures or exceptions to lack of novelty" and furnish that statement below.*

CONTINUATION OF BOX NO.IV

COLLINGWOOD, Anthony Robert
GRAHAM, John George
GRATWICK, Christopher
GIBSON, Sara Hillary Margaret
HUMPHRIES, Martyn
MILLROSS, Christopher Robert
ROBERTS, Jonathan Winstanley
THOMAS Ieuan

Box No. VI PRIORITY CLAIM ☐ Further priority claims are indicated in the Supplemental Box.

Filing date of earlier application (day month year)	Number of earlier application	Where earlier application is: national application: country	regional application:* regional Office	international application: receiving Office
item (1) 7.7.1998 7 July 1998	9814653.3	GB		
item (2)				
item (3)				

☒ The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) *(only if the earlier application was filed with the Office which for the purposes of the present international application is the receiving Office)* identified above as item(s): (1)

* *Where the earlier application is an ARIPO application, it is mandatory to indicate in the Supplemental Box at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed (Rule 4.10(b)(ii)). See Supplemental Box.*

Box No. VII INTERNATIONAL SEARCHING AUTHORITY

Choice of International Searching Authority (ISA) *(if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used):*
ISA /

Request to use results of earlier search; reference to that search *(if an earlier search has been carried out by or requested from the International Searching Authority):*
Date *(day month year)* Number Country *(or regional Office)*

Box No. VIII CHECK LIST; LANGUAGE OF FILING

This international application contains the following **number of sheets:**

request	:	5
description (excluding sequence listing part)	:	12
claims	:	1
abstract	:	1
drawings	:	
sequence listing part of description	:	1
Total number of sheets	:	20

This international application is **accompanied by** the item(s) marked below:

1. ☒ fee calculation sheet
2. ☒ separate signed power of attorney (To Follow)
3. ☐ copy of general power of attorney; reference number, if any:
4. ☐ statement explaining lack of signature
5. ☐ priority document(s) identified in Box No. VI as item(s):
6. ☐ translation of international application into (language):
7. ☒ separate indications concerning deposited microorganism or other biological material
8. ☐ nucleotide and/or amino acid sequence listing in computer readable form
9. ☒ other *(specify)*: FORM 23/77

Figure of the drawings which should accompany the abstract:

Language of filing of the international application: ENGLISH

Box No. IX SIGNATURE OF APPLICANT OR AGENT

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).

M. Humphries

MARTYN HUMPHRIES
AUTHORISED OFFICER

For receiving Office use only

1. Date of actual receipt of the purported international application:
2. Drawings: ☐ received: ☐ not received:
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:
4. Date of timely receipt of the required corrections under PCT Article 11(2):
5. International Searching Authority (if two or more are competent): ISA /
6. ☐ Transmittal of search copy delayed until search fee is paid.

For International Bureau use only

Date of receipt of the record copy by the International Bureau:

This sheet is not part of and does not count as a sheet of the international application.

PCT

FEE CALCULATION SHEET

Annex to the Request

For receiving Office use only

International application No.

Date stamp of the receiving Office

Applicant's or agent's file reference: MTW 50632/WO

Applicant: QUEST INTERNATIONAL B.V.

CALCULATION OF PRESCRIBED FEES

1. TRANSMITTAL FEE . . . . . 55.00 [T]

2. SEARCH FEE . . . . . 812.00 [S]

International search to be carried out by _____

(If two or more International Searching Authorities are competent in relation to the international application, indicate the name of the Authority which is chosen to carry out the international search.)

3. INTERNATIONAL FEE

Basic Fee

The international application contains 20 sheets.

first 30 sheets . . . . . 285.00 [b1]

_____ (remaining sheets) x _____ (additional amount) = [b2]

Add amounts entered at b1 and b2 and enter total at B . . . . 285.00 [B]

Designation Fees

The international application contains ALL designations.

10 (number of designation fees payable *(maximum 10)*) x 65.00 (amount of designation fee) = 650.00 [D]

Add amounts entered at B and D and enter total at I . . . . . 935.00 [I]

(Applicants from certain States are entitled to a reduction of 75% of the international fee. Where the applicant is (or all applicants are) so entitled, the total to be entered at I is 25% of the sum of the amounts entered at B and D.)

4. FEE FOR PRIORITY DOCUMENT *(if applicable)* . . . . . 22.00 [P]

5. TOTAL FEES PAYABLE . . . . . 1824.00 TOTAL

Add amounts entered at T, S, I and P, and enter total in the TOTAL box

[ ] The designation fees are not paid at this time.

MODE OF PAYMENT

[X] authorization to charge deposit account (see below)
[ ] bank draft
[ ] coupons
[ ] cheque
[ ] cash
[ ] other *(specify)*:
[ ] postal money order
[ ] revenue stamps

DEPOSIT ACCOUNT AUTHORIZATION *(this mode of payment may not be available at all receiving Offices)*

The RO/ 101

[X] is hereby authorized to charge the total fees indicated above to my deposit account.

[X] *(this check-box may be marked only if the conditions for deposit accounts of the receiving Office so permit)* is hereby authorized to charge any deficiency or credit any overpayment in the total fees indicated above to my deposit account.

[X] is hereby authorized to charge the fee for preparation and transmittal of the priority document to the International Bureau of WIPO to my deposit account.

2805 0210 — Deposit Account No.

5 July 1998 — Date *(day/month/year)*

Signature

Applicant's or agent's file reference number [redacted]50632	International application No. [redacted]

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13*bis*)

A. The indications made below relate to the microorganism referred to in the description on page 6, line 17-19

B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet ☐

Name of depositary institution

NATIONAL COLLECTIONS OF INDUSTRIAL AND MARINE BACTERIA LTD.

Address of depositary institution *(including postal code and country)*

23 ST MACHAR DRIVE
ABERDEEN
SCOTLAND
UNITED KINGDOM

Date of deposit	Accession Number
28 JUNE 1999 (provisional)	NCIMB 13590

C. ADDITIONAL INDICATIONS *(leave blank if not applicable)* This information is continued on an additional sheet ☐

D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE *(if the indications are not for all designated States)*

E. SEPARATE FURNISHING OF INDICATIONS *(leave blank if not applicable)*

The indications listed below will be submitted to the International Bureau later *(specify the general nature of the indications e.g., "Accession Number of Deposit")*

For receiving Office use only	For International Bureau use only
☐ This sheet was received with the international application	☐ This sheet was received by the International Bureau on:
Authorized officer	Authorized officer

15

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
MTW50632/WO		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB99/02165	06/07/1999	07/07/1998
International Patent Classification (IPC) or national classification and IPC A61K7/32		
Applicant QUEST INTERNATIONAL B.V. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 1 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
21/01/2000	24.10.2000
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Adechy. M Telephone No. +49 89 2399 8576

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB99/02165

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-12	as originally filed	

Claims, No.:

1-12	as originally filed	
13-15	with telefax of	16/08/2000

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
- ☒ claims Nos. 6, 7, 8.

because:

- ☒ the said international application, or the said claims Nos. 6, 7, 8 relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	14-15
	No:	Claims	1-13
Inventive step (IS)	Yes:	Claims	14
	No:	Claims	1-13, 15
Industrial applicability (IA)	Yes:	Claims	1-5, 9-15
	No:	Claims	

2. Citations and explanations

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item III

Non establishment of opinion with regard to industrial applicability

Claims 6, 7 and 8 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item V

Reasoned statement under Art. 35 (2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1) Reference is made to the following documents:

D1: US-A-5 554 588
D2: XP002120135

2) Novelty Art. 33 (1) and (2) PCT:

The subject matter of Claims 1, 6, 7, 8, 9, 10 and 11, concerns respectively a cosmetic method for preventing or reducing body malodour, the use of a perfume component, the use of a perfume composition or the use of a deodorant both comprising such a component , for the above purpose, as well as products such as deodorant product and perfume composition and a method for producing such a perfume composition. The subject matter of the above claims lacks novelty in the light of D1 (e.g. p.1 lines 6-17, p. 3 lines 40-60, p. 4 line 66, p. 12 Table 2, p. 14 Table I, p. 15, p. 16 Table IV), which also discloses a method of reducing or preventing body malodour by means of a fragrance composition comprising a specific perfume component (having bactericide properties). Such products (perfume components, perfume composition, deodorant, also their use and a method for producing a perfume composition, are described in the said document where all the technical features are found (e.g. nature and proportion of the perfume component). In the case of Claim 6, the inactivation of corynebacteria is regarded as a result of the method applied to reduce body malodour, and not as a technical feature, therefore the subject matter of the said claim is known from D1.

The same applies to their respective dependant Claims 2-5 and 12, of which the subject matter is disclosed in D1.

It must be stressed that, although examples 1 to 4 and 5 to 8 of D1 discloses perfume components of the claims at individual level lower than 30%, the said document states on page 4 that the amount of individual compounds is at least 2% of the perfume composition, and also that the amount of total alcohol can reach 50%. Therefore, the subject matter of claim 13 (concerning a perfume composition comprising at least 30% of one or more of specific components) can fall within the value given and is not regarded as novel in the light of D1.

The subject matter of claims 14 and 15, concerning perfume compositions comprising 60% of one, or more, components listed (14) and 30 % of at least 5 components (15), is not disclosed in the prior art documents as the documents do not disclose that a perfume composition comprise 60% of the claimed component and also less than 5 of the claimed components were found in D1. Claims 14 and 15 are therefore regarded as novel.

3) Inventive step Art. 33 (1) and (3) PCT:

The closest prior art is viewed as D1, disclosing the subject matter of the present invention, as well as the technical features. It differs from the present invention in that it does not specifically refers to corynebacteria and also in terms of technical features.

The subject matter of claim 14 is regarded as involving an inventive step because the description does show that an odour reduction is obtained more efficiently when the percentage of perfume components listed is higher.

The subject matter of claim 15 is not regarded as involving an inventive step as it does not show which technical problem is solved having at leas 5 perfume components claimed.

4) Industrial applicability

For the assessment of the present claims 6, 7 and 8 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item VIII

Certain observations on the international application

1) The large number of independent claims renders the scope where protection is sought unclear Art 6 PCT.

2) The description does not refer to prior art document D1 which is relevant to the present invention (Rule 5.1 (ii) PCT).

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION**	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
MTW50632/WO		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/GB 99/02165	06/07/1999	07/07/1998
Applicant		
QUEST INTERNATIONAL B.V. et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

[ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

[ ] contained in the international application in written form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readble form.

[ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [ ] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

[X] the text is approved as submitted by the applicant.

[ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**

[X] the text is approved as submitted by the applicant.

[ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. _____

[ ] as suggested by the applicant.

[ ] because the applicant failed to suggest a figure.

[ ] because this figure better characterizes the invention.

[ ] None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 99/02165

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K7/32 A61K7/46

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 554 588 A (BEHAN JOHN M ET AL) 10 September 1996 (1996-09-10) abstract column 1, line 60 -column 2, line 3 examples 5-8 column 16, line 1 -column 17, line 9 claims 12,20,21	1-4,9,10

X	LACOSTE, E. ET AL.: "LES PROPRIETES ANTISEPTIQUES DE L'HUILE ESSENTIELLE DE LIPPIA SIDOIDES CHAM. APPLICATION A LA MICROFLORE CUTANEE" ANN. PHARMACEUTIQUES FRANÇAISES, vol. 54, no. 5, 1996, pages 228-230, XP002120135 the whole document	1,5,6,8
Y		3

	-/--	

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
4 November 1999	16/11/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Cielen, E

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
Y	MORRIS J A ET AL: "ANTIMICROBIAL ACTIVITY OF AROMA CHEMICALS AND ESSENTIAL OILS" JOURNAL OF THE AMERICAN OIL CHEMISTS' SOCIETY,1 May 1979 (1979-05-01), pages 595-603, XP000645444 ISSN: 0003-021X page 595, paragraph 1 - paragraph 3 table III	3
Y	FIEDLER, H. P.: "ANTIMIKROBIELLE WIRKUNG VON AROMASTOFFEN UND AETHERISCHE ÖLE" SEIFEN-ÖLE-FETTE-WACHSE, vol. 107, no. 3, 1981, pages 15-76, XP002120136 page 75 -page 76	3
A	GB 1 575 380 A (DRAGOCO GERBERDING CO GMBH) 24 September 1980 (1980-09-24) the whole document	1,4
A	EP 0 126 944 A (DRAGOCO GERBERDING CO GMBH) 5 December 1984 (1984-12-05) abstract page 1, paragraph 1 - paragraph 2 page 3, paragraph 1 - paragraph 3 table 1 page 7, paragraph 3	1,11
A	US 5 420 104 A (HOLZNER GUENTER ET AL) 30 May 1995 (1995-05-30) abstract column 1, line 5 - line 17 column 1, line 58 -column 2, line 7 column 3, line 16 - line 67 column 5, line 3 - line 8 column 6, line 7 - line 51 claims	

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/GB 99/02165

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5554588 A	10-09-1996	CA 2082281 A,C	09-05-1993
		DE 69221087 D	04-09-1997
		DE 69221087 T	13-11-1997
		EP 0545556 A	09-06-1993
		ES 2104850 T	16-10-1997
		JP 5255689 A	05-10-1993
		MX 9206423 A	01-05-1993
		ZA 9208578 A	06-05-1994
GB 1575380 A	24-09-1980	DE 2653186 A	24-05-1978
		AT 350727 B	11-06-1979
		AT 548277 A	15-11-1978
		FR 2371192 A	16-06-1978
		IT 1081119 B	16-05-1985
EP 0126944 A	05-12-1984	DE 3315058 A	31-10-1984
		AT 46817 T	15-10-1989
		JP 1612109 C	30-07-1991
		JP 2040043 B	10-09-1990
		JP 60064913 A	13-04-1985
US 5420104 A	30-05-1995	DE 69305615 D	28-11-1996
		DE 69305615 T	20-02-1997
		WO 9325185 A	23-12-1993
		EP 0600060 A	08-06-1994
		JP 6509816 T	02-11-1994

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PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 : A61K 7/32, 7/46

A1

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(30) Priority Data:
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(71) Applicant *(for all designated States except US)*: QUEST INTERNATIONAL B.V. [NL/NL]; Huizerstraatweg 28, NL–1411 GP Naarden (NL).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: WILSON, Craig, Stewart [GB/GB]; 30 Tilden Close, High Halden, Kent TN26 3LR (GB). MINHAS, Tony [GB/GB]; 30 King Edward Avenue, Dartford, Kent DA1 2HZ (GB). BEHAN, John, Martin [GB/GB]; The Forge, The Green, Boughton Aluph, Ashford, Kent TN25 4JB (GB).

(74) Agents: HUMPHRIES, Martyn et al.; ICI Group Intellectual Property, P.O. Box 90, Wilton, Middlesbrough, Cleveland TS90 8JE (GB).

(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.
With an indication in relation to deposited biological material furnished under Rule 13bis separately from the description.

(54) Title: METHOD OF REDUCING OR PREVENTING MALODOUR

(57) Abstract

A method for reducing or preventing body malodour by topically applying to human skin perfume components capable of inhibiting the production of malodorous metabolites caused by micro–organisms comprising corynebacteria. The perfume components are capable of inactivating corynebacteria capable of catabolising fatty acids.

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METHOD OF REDUCING OR PREVENTING MALODOUR

This invention relates to perfume components, mixtures thereof and perfume compositions, to personal products and detergent products containing such perfumes, and to a method and the use of such perfumes and products to deliver a deodorant effect.

In particular, it relates to perfume components, mixtures thereof, and perfume compositions for inhibiting the production of odorous metabolites by topically applying to human skin perfumery components capable of inhibiting the production of body malodour caused by micro-organisms comprising corynebacteria, preferably by selectively inhibiting those corynebacteria capable of catabolising fatty acids.

It is well known that freshly secreted sweat is odourless and that body malodour is the result of a biotransformation of the sweat by micro-organisms living on the surface of the skin to produce volatile odoriferous compounds.

There are three types of personal product routinely used to combat body malodour: perfumes, antiperspirants and deodorants.

Perfumes may simply mask body malodour. However perfume compositions have been disclosed which exhibit a deodorant action. EP-B-3172, EP-A-5618, US-A-43044679, US-A-4322308, US-A-4278658, US-A-4134838, US-A-4288341 and US-A-4289641 all describe perfume compositions which exhibit a deodorant action when applied to human skin or when included in a laundry product used to launder textiles.

Antiperspirants work by blocking the sweat glands thereby reducing perspiration.

Antimicrobial agents used in deodorants are designed to reduce the population of micro-organisms living on the surface of the skin. Typical agents of this nature include ethanol and Triclosan (2,4,4'-trichloro-2'-hydroxy-diphenyl ether) which are well known to exert antimicrobial effects. The use of common deodorant actives results in a non-selective antimicrobial action exerted upon most of the skin's natural microflora. This is an undesirable side effect of such deodorant formulations.

Many disclosures describe compositions comprising antimicrobials which are designed to eliminate malodour by sub-lethally reducing the microflora population.

WO 95/16429 (Henkel) describes deodorant compositions comprising fat soluble partial esters of hydroxy carboxylic acids.

WO 95/07069, WO 91/11988 and WO 91/05541 (all Gillette) describe deodorant compositions comprising inhibitors of pyridoxal phosphate dependent amino acid lyase.

WO 94/14934 (Unilever) describes a method for reducing the perceptibility of an odoriferous substance using an antibody or antibody fragment. Such antibodies could be used in deodorant compositions.

WO 93/07853 (Monell) describes the use of mimics of the odoriferous compound 3-methyl-2-hexenoic acid to reduce body malodour.

DD 29 39 58 (Medezinische Fakultaet (Charite) der Humboldt Universitaet zu Berlin) describes the use of lipoxygenase inhibitors to act biochemically to reduce sweat production or to inhibit, to various degrees, the action of skin bacteria or their enzymes on the

decomposition of sweat to form unpleasant-smelling substances.

DE 43 43 265 (Henkel) describes deodorant compositions comprising saturated dioic acid (C3 - C10) esters. It is claimed that the active inhibits a sweat decomposing esterase and the compositions are said not to disturb the skin's natural microflora.

DE 43 43 264 (Henkel) describes the use of lipid-soluble partial esters of hydroxy carboxylic acids in deodorant compositions.

Some disclosures describe the use of antimicrobial substances which are selective against odour producing bacteria.

WO 90/15077 (Gillette) describes the use of antibodies to a carrier or transport protein of coryneform and staphylococci. It is disclosed that these bacteria types have an amino acid lyase enzyme which is responsible for the formation of malodour.

DE 43 39 605 (Beiersdorf) describes the use of deodorising mixtures of alpha-omega alkanedioic acids and fatty acid partial glycerides of unbranched fatty acids which may be present in a suitable cosmetic vehicle to combat Gram-positive, particularly coryneform, bacteria.

Woolwax acids have also been disclosed in the following Beiersdorf publications as deodorant actives in combination with:

-alpha-omega alkanedioic acids (DE 43 24 219);

-partial glycerides of unbranched fatty acids (DE 43 09 372); or

-monocarboxylic acids, especially unbranched fatty acids (DE 43 05 889).

Each combination is described as suitable to combat Gram-positive, especially coryneform bacteria.

DE 4237081 (Beiersdorf) describes deodorant compositions comprising monocarboxylic acid diglycerides and/or triglycerides. The compositions are said to be suitable against Gram-positive, especially coryneform, bacteria.

EP-A-0 697 213 (Beiersdorf) describes the selective reduction of coryneform bacteria using a mixture of:

-lauric acid;

-one other fatty acid C6 - C20 (one of which must be at least C12);

-glyceryl monocaprate/glyceryl monocaprylate;

-without the use of ethoxylated glyceryl fatty acid esters and propoxylated glyceryl fatty acid esters;

which has a pH of less than 8.

WO 94/07837 (Unichema) describes certain novel unsaturated dioic acids having between 8 and 22 carbon atoms. Also described is their potential use to treat malodour.

EP-A-0 750 903 (Cooperatie Cosun UA) discloses deodorant compositions comprising sugar-fatty acid esters. The actives are described as being selective towards odour causing micro-organisms. These odour-causing micro-organisms are said to be the Corynebacterium varieties known as lipophilic diphtheroids such as *Corynebacterium xerosis* and *C. minutissimum.*

Coryneform is a designation of a large ill-defined group of bacteria. The diverse genera that have been included with the coryneforms include Actinomyces, Arachnia, Arcanobacterium, Arthrobacter, bacterionema, Bifidobacterium, Brevibacterium, Cellulomonas, Corynebacterium, Eyrsipelothrix, Eubacterium, Kurthia, Listeria, Mycobacterium, Nocardia, Oerskovia, Propionibacterium, Rhodococcus and Rothia.

It is clear that the majority of previous disclosures in this area have been aimed at antibacterial or bacteriostatic effects towards the whole skin flora or selected species.

Without being bound by theory we believe that the *Corynebacterium* genus can be subdivided into two subgroups according to ability to catabolise fatty acids. We further believe that one of these subgroups, hereinafter referred to as "Corynebacteria A", which is capable of catabolising fatty acids, contributes strongly to the formation of body malodour, in particular axillary malodour. The other subgroup, hereinafter referred to as "Corynebacteria B", which catabolises fatty acids much less so or not at all, contributes much less or even not at all to malodour formation. We also believe that it is possible to selectively inhibit the generation of odorous metabolites by Corynebacteria A.

The deodorants available on the market tend to be insufficiently effective and/or substantially reduce the numbers of all bacteria in the microflora indiscriminately. The present invention offers the opportunity to provide deodorant products which for many females will substantially reduce malodour formation while inhibiting only a minor portion of the microflora. For many males malodour formation can be substantially reduced or even largely eliminated by inactivating the Corynebacteria A.

Furthermore, we have found a range of perfume components capable of selectively inactivating Corynebacteria A, while leaving other bacteria, notably Corynebacteria B much less affected or even not notably affected at all. Significant deodorant action can be obtained by the action of these components singly or in combination.

Accordingly, the invention provides a cosmetic method for reducing or preventing body malodour by topically applying to human skin a composition comprising an active agent capable of inactivating body malodour-causing micro-organisms comprising corynebacteria, wherein the agent is a perfume component which is capable of inactivating the corynebacteria capable of catabolising fatty acids.

The invention also provides the use of a perfume component to inactivate the corynebacteria capable of catabolising fatty acids.

The invention further provides the use of a perfume composition, comprising at least 30% by weight of one or more perfume components capable of inactivating the corynebacteria capable of catabolising fatty acids, to reduce body malodour.

The invention further provides the use of a deodorant product comprising a perfume component to reduce body malodour by inactivating the corynebacteria capable of catabolising fatty acids.

The invention further provides a perfume composition comprising at least 30% by weight of one or more of the following perfume components;

(Z)-3,4,5,6,6-pentamethylhept-3-en-2-one, mixtures of diethyl- and dimethyl-cyclohex-2-en -1-one, citronellol, 2-methyl-3-(4-(1-methylethyl)phenyl)propanal, (2-(methyloxy)-4-propyl -1-benzenol), diphenylmethane, tetrahydrolinalol, 4-(4-methyl-3-pentenyl)cyclohex-3-ene -1-carbaldehyde, 3-(4-methyl-3-pentenyl)cyclohex-3-ene-1-carbaldehyde, 3-(1,3-benzodioxol -5-yl)-2-methylpropanal, α-ionone, β-ionone, tricyclo[5.2.1.0,2,6]dec-4-en-8-yl ethanoate, 4-(4-hydroxy-4-methylpentyl)cyclohex-3-enecarbaldehyde, 3-(4-hydroxy-4-methylpentyl) -cyclohex-3-enecarbaldehyde, methyl iso-eugenol, 2-(1,1-dimethylethyl)cyclohexyl ethanoate, 4-(1,1-dimethylethyl)cyclohexylethanoate, 4-methyl-2-(2-methylprop-1-enyl) tetrahydropyran, and a deodorant product comprising such a perfume composition.

The invention still further provides a method of producing a perfume composition which comprises (i) evaluating perfume components on the ability to inhibit fatty acid metabolism in corynebacteria, (ii) selecting perfume components on the ability to sub-lethally inhibit fatty acid metabolism in corynebacteria, and (iii) mixing together two or more of said selected perfume components, optionally with other perfume components.

The term "perfume component" is used herein to represent a material which is added to a perfume to contribute to the olfactive properties of the perfume. A perfume component can be acceptably employed to provide odour contributions to the overall hedonic performance of products. Typically, a perfume component will be generally recognised as possessing odours in its own right, will be relatively volatile and often has a molecular weight within the range 100 to 300. Typical materials which are perfume components are described in "Perfume and Flavour Chemicals", Volumes I and II (Steffan Arctander, 1969). A perfume composition will contain a number of individual perfume components, and optionally a suitable diluent. The concentration of perfume components referred to herein is relative to the total concentration of perfume components present in the composition, ie excludes any diluent.

The perfume components used in the present invention are capable of inactivating Corynebacteria, preferably selectively inactivating Corynebacteria A. By inactivate is meant any sub-lethal effect resulting in a reduction or elimination of the production of odoriferous metabolites, eg by modification of bacterial metabolism, such as fatty acid metabolism. The sub-lethal effect of a perfume component preferably occurs at concentrations below its minimum inhibitory concentration, determined as decribed in Example 2 below.

In particular, by sub-lethal is meant a significant inhibition of metabolism, e.g. pentadecanoic acid utilisation (at least 60% inhibition), preferably without concomitant reductions in cell viability (not more than 1 $\log_{10}$ CFU/ml reduction) and glucose utilisation (not more than 10% reduction).

The perfume components used in the present invention may be incorporated into deodorant products which include, but are not limited to, body deodorants and antiperspirants including roll ons, gel products, stick deodorants, antiperspirants, shampoos, soap shower gels, talcum powder, hand cream, skin conditioners, sunscreen, sun tan lotion, skin and hair conditioners.

The perfume components may also be usefully employed for deodorant properties by incorporation into other products, for example, in laundry and household products such as

rinse conditioners, household cleaners and detergent cleaners. The perfume components can b incorporated into textiles themselves during their production using techniques known in the art, to provide deodorant protection.

It is postulated that the preferred selective inhibition of Corynebacteria A is achieved by inhibiting the metabolic pathways of the Corynebacteria A which leads to a reduction in the production of malodorous metabolites. The inhibition of the metabolic pathway of Corynebacteria A is more important than the inhibition of the metabolic pathway of Corynebacteria B, as only the Corynebacteria A are capable of producing malodorous products.

In a preferred method according to the invention, perfume components which selectively inhibit the metabolic pathway of only those corynebacteria capable of catabolising fatty acids are used, by which is meant inactivating Corynebacteria A to a significantly higher degree than Corynebacteria B. Preferably, it means inactivating Corynebacteria A to a significantly higher degree than the majority, preferably at least 75%, more preferably at least 90% of bacteria, other than Corynebacteria A constituting the skin microflora.

The levels of perfume materials used in a skin product may lead to general bacteriostatic and bactericidal effects. A skilled person responsible for formulating a finished product will be able to adjust the level to produce the desired effect in the final product.

The perfume components employed in the present invention are more active with Corynebacteria A than with other bacteria constituting the axillary microflora, including Corynebacteria B, when considering the selective inhibition of the metabolic pathway of the bacteria, particularly in respect of fatty acid metabolism.

The active perfume components preferably selectively inhibit the metabolic pathway of Corynebacteria A, leading to a reduction of malodorous compounds, producing a deodorant effect in consumer products. In a preferred method according to the invention, an Odour Reduction Value, measured as described in Example 4, of at least 10%, more preferably at least 30%, and particularly at least 50% is obtained. The active components may be mixed with other perfume components to deliver perfumes or perfume compositions with the desired deodorant and hedonistic properties. To deliver high deodorant effects the active components preferably comprise 30% or more of the total perfume formulation by weight, more preferably at least 40% and particularly at least 60%. A deodorant product preferably comprises at least 0.05% to 4%, more preferably 0.1% to 2% by weight of the active perfume components. Preferred actives include the following perfume components.

(Z)-3,4,5,6,6-pentamethylhept-3-en-2-one (Acetyl di iso amylene)

Mixture of diethyl- and dimethyl-cyclohex-2-en-1-one (Azarbre)

Citronellol

2-methyl-3-(4-(1-methylethyl)phenyl)propanal (Cyclamen aldehyde)

(2-(methyloxy)-4-propyl-1-benzenol) (Dihydroeugenol)

Diphenylm thane

Tetrahydrolinalol

4-(4-methyl-3-pentenyl)cyclohex-3-ene-1-carbaldehyde (Empetaal)

3-(4-methyl-3-pentenyl)cyclohex-3-ene-1-carbaldehyde (Empetaal)

3-(1,3-benzodioxol-5-yl)-2-methylpropanal (Helional)

α- and β-Ionone and mixtures thereof (Ionone)

tricyclo[5.2.1.0 2,6]dec-4-en-8-yl ethanoate (Jasmacylene)

4-(4-hydroxy-4-methylpentyl)cyclohex-3-enecarbaldehyde (Lyral)

3-(4-hydroxy-4-methylpentyl)cyclohex-3-enecarbaldehyde (Lyral)

Methyl iso-eugenol

2-(1,1-dimethylethyl)cyclohexyl ethanoate (Ortholate)

4-(1,1-dimethylethyl)cyclohexyl ethanoate (Ortholate)

4 -Methyl-2-(2-methylprop-1-enyl)tetrahydropyran (Rose oxide)

A perfume composition for use in the present invention preferably comprises at least 5, more preferably at least 10, and particularly at least 15 of the above perfume components.

The invention is illustrated by the following examples.

EXAMPLE 1

A demonstration of fatty acid catabolism in an isolated pure culture of Corynebacterium A deposited as NCIMB 13590 (deposited under the Budapest Treaty with National Collections of Industrial and Marine Bacteria Ltd, 23 St Machar Drive, Aberdeen Scotland, UK on 28 June 1999) was determined *in vitro* using the method given below:

The *in vitro* model system, reproducing fatty acid catabolism by axillary bacteria, consisted of 250 ml baffled shake flasks, to which were added 30 ml semi-synthetic medium (see below) supplemented with fatty acid substrate (2.0 mg/ml pentadecanoic acid) This system was employed to evaluate selected potential deodorant actives (see below). Flasks were inoculated with fresh bacterial biomass, pre-grown for 24 h in TSBT (see below), to give starting optical densities (A_{580}) of 1.0 - 2.0. Following inoculation, flasks were incubated aerobically at 35°C, with agitation (130 rpm), and analysed after 24 h. Culture viability/purity was determined by TVC analysis on TSAT plates (see below) following serial dilution in quarter-strength Ringers solution.

Fatty acid levels in the flasks were determined by capillary gas chromatography (GC) analysis. Initially, 5.0 ml aliquots from each flask were rapidly transferred into universal tubes; an internal standard (1.0 mg/ml lauric acid) was added to each universal tube and the culture medium was acidified (pH ~2) by the addition of hydrochloric acid. Liquid-liquid extraction was then carried out using 2 vol (10 ml) ethyl acetate; organic and aqueous phases were resolved by centrifugation (2000 rpm, 3 min). 2.0 ml of each organic (upper) phase was then transferred to a sampling tube prior to analysis on a Perkin Elmer 8000 (Series 2) GC fitted with a 15 m x 0.32 mm (internal diameter) FFA (nitroterephthalic acid modified PEG/siloxane copolymer) fused silica capillary column (film thickness 0.25 mm) (Quadrex). This column was attached to the split splitless injector and flame ionisation detector (FID) of the GC ; injector and detector temperatures were each 300°C. Carrier gas for the column was helium (6.0 psi), while hydrogen (17 psi) and air (23 psi) were supplied the FID. The temperature programme for fatty acid analysis was 80°C (2 min); 80-250°C (20°C/min); 250°C (5 min). Sample size for

injection was 0.5 -1.0 µl. Fatty acid levels in the flasks were quantified by comparison of peak areas with known levels of both internal (lauric acid) and external (pentadecanoic acid) standards.

EXAMPLE 2

The minimum inhibitory concentration of perfume components was determined by the following method.

A fresh culture of of the test inoculum (Corynebacteria xerosis NCTC 7243 (National Collection of Type Cultures, Public Health Laboratory Service, Central Public Health Laboratory , 61 Colindale Avenue, London)) diluted in sterile 0.1% special peptone solution to give a concentration of approximately 10^6 cfu/ml was prepared.

Test samples were diluted in sterile trptone soya broth (TSB) Each row of the microtitre plate (labelled A - H) was allocated to one sample, i.e. eight samples per plate. Row 8 (H) contained only TSB for use as a bacterial control to indicate level of turbidity in the absence of test material. Aseptically 200 µl of the initial dilution was transferred to the 1st and 7th well of the appropriate row. All other test wells were filled with 100 µl of sterile TSB using an 8 channel pipette. The contents of all wells in column 1 were mixed by sucking samples up and down pipette tips before 100 µl was transferred to column 2. The same sterile pipette tips can be used to transfer 100 µl of each well in column 7 in to the appropriate well in column 8. Tips were discarded into disinfectant solution. Using fresh sterile tips the process was repeated by transferring 100 µl from column 2 into column 3 (and 8 into 9). The process was continued until all wells in columns 6 and 12 contained 200 µl. After mixing 100 µl was discarded from wells in these columns to waste.

To all wells 100 µl of pre-diluted test culture was added giving 200 µl final volume in each well.

A blank plate was prepared for each set of samples using the above protocol except 100 µl of sterile 0.1% peptone was added instead of bacterial culture.

Plates were sealed using autoclave tape and incubated overnight at 35° C.

The reader was preset to gently agitate the plates to mix the contents before reading absorbance at 540 nm. The control plate for each set of samples was read first. The reader was then reprogrammed to use the control readings to blank all other plate readings of the set of test materials (i.e. removing turbidity due to perfume and possible colour changes during incubation) thus only printing out absorbances due to turbidity resulting from bacterial growth. Limits were set so that degrees of turbidity were given a rating.

The MIC was taken as the level of sample required to inhibit growth completely (change in absorbance < 0.2).

EXAMPLE 3

Demonstration of sub-lethal inactivation of fatty acid catabolism was performed with the following in *vitro* method.

Prior to inoculation, flasks were supplemented with selected perfume components, at a range of concentrations (eg 500 ppm and 1000 ppm) below their predetermined minimum inhibitory concentration, to determine their ability to sub-lethally inhibit fatty acid catabolism by

Corynebacteria A (NCIMB 13590). Stock active solutions/emulsions were prepared in semi-synthetic medium (see below), emulsions were formed by ultra-homogenisation at 24,000 rpm for ~1 min. At the end of each experiment, viability and fatty acid levels in the experimental flasks were compared to those in a control flask. Sub-lethal inhibition of fatty acid catabolism was defined as significant inhibition of pentadecanoic acid utilisation, without concomitant reductions in cell viability.

Composition of Tween-supplemented Tryptone soya broth/agar (TSBT, TSAT) used for growth/maintenance of axillary bacteria (g/l) :Tryptone soya broth (30.0), Yeast extract (10.0), Tween 80 (1.0), ± Agar (20.0). Composition of semi-synthetic medium used in laboratory systems simulating fatty acid catabolism by axillary bacteria (g/l): KH_2PO_4 (1.6), $(NH_4)_2HPO_4$ (5.0), Na_2SO_4 (0.38), Yeast Nitrogen Base (Difco) (3.35), Yeast Extract (0.5), Tween 80 (0.2), Triton X-100 (0.2), $MgCl_2.6H_20$ (0.5), Pentadecanoic acid (2.0).

The results below show the perfume components that are active and inactive with regard to the inhibition of fatty acid metabolism in Corynebacteria A.

Inhibition of long chain fatty acid metabolism observed	**No inhibition of long chain fatty acid metabolism observed**
(Z)-3,4,5,6,6-pentamethylhept-3-en-2-one	Aldehyde C11
Mixture of diethyl- and dimethyl-cyclohex-2-ene-1-one	Anisic Aldehyde
2-methyl-3-(4-(1-methylethyl)phenyl) propanal	Caryophyllene
(2-(methyloxy)-4-propyl-1-benzenol)	Cinnamic alcohol
Diphenylmethane	2H-2-chromenone
4-(4-methyl-3-pentenyl)cyclohex-3-ene-1-carbaldehyde	
3-(4-methyl-3-pentenyl)cyclohex-3-ene-1-carbaldehyde	Florocyclene 3a,4,5,6,7,7a-hexahydro-4,7-methano-1H-inden-6-yl propanoate
3-(1,3-benzodioxol-5-yl)-2-methylpropanal	4,6,6,7,8,8-hexamethyl-1,3,4,6,7,8-hexahydrocyclopenta[gamma]isochromene
Mixture of alpha and beta ionone	Hexyl cinnamic aldehyde
4-(4-hydroxy-4-methylpentyl)cyclohex-3-ene carbaldehyde	
3-(4-hydroxy-4-methylpentyl)cyclohex-3-ene carbaldehyde	hexyl 2-hydroxy-1-benzene carboxylate

Methyl-iso-eugenol	Iso-e-super
2-(1,1-dimethylethyl)cyclohexyl ethanoate	Lilial
4-Methyl-2-(2-methylprop-1-enyl)-tetrahydropyran	Thyme red

EXAMPLE 4

The following are typical formulations of deodorant products which comprise a perfume or perfume component capable of inhibiting the production of body malodour by micro-organisms comprising Corynebacteria. These formulations are made by methods common in the art.

Deodorant Sticks

Ingredient	Content (% by weight)	
	Formulation 1A	Formulation 1B
Ethanol		8
Sodium Stearate	7	6
Propylene glycol	70	12
Perfume	1.5	2
PPG-3 Myristyl ether		28
PPG-10 Cetyl ether		10
Cyclomethicone		34
Silica		
Water	21.5	

Aerosols

Ingredient	content % by weight	
	Formulation 2A	Formulation 2B
Ethanol B	up to 100	
Propylene glycol	as required	
Perfume	2.5	1.5
Chlorhydrol microdry		31.8
Silicone Fluid DC344		up to 100
Bentone gel IPP		13.65

Irgasan DP300	0.03	
Dimethyl ether	20	
Concentrate		22
Water	23	

Roll ons

Ingredient	Content % by weight	
	Formulation 3A	Formulation 3B
Ethanol	to 100%	60
Klucel MF		0.65
Cremphor RM410		0.5
Perfume	0.5	1
AZTC*	20	
Cyclomethicone	68	
Dimethicone	5	
Silica	2.5	
Water		37.85

* Aluminium zirconium tetrachlorohydro glycinate

Two perfume compositions embodying this invention were made and tested for deodorant action in an underarm product, using an Odour Reduction Value test generally as described in US-A-4278658, but with the substitution of the perfumed soap by perfumed roll-on product, using the formulation described in Formulation 3B. These perfume compositions and the method for an Odour Reduction Value test are set out below.

	Composition by %	
	Perfume A	Perfume B
Acetyl di iso amylene	10	7
Adoxal		0.5
Amberlyn super PM 577 10%DPG	3	
Azarbre	3.5	
Benzyl acetate extra	8	8
Benzyl salicylate	8	12

Cassis base		5
Citral lemarome		3
Citronellol pure		15
Cyclamen aldehyde		5
Dihydro jasmone	0.5	
Diphenyl methane	3	
Dupical		0.3
Helional		4
Ionone	15	
Jasmacyclene	3	
Ligustral 10%DPG AAA 1486	3	
Lyral	8	15
Methyl iso eugenol	5	
Methyl octyl acetaldehyde 10%DPG AA1918		2
Ortholate		8
Para tert butyl cyclo hexyl acetate	12	
Phenyl ethyl alcohol	12	13
Roseacetone	6	2.2

The Odour Reduction Value test was carried out using a panel of 40 Caucasian male subjects. A standard quantity (approximately 0.4g) of a roll-on product containing one of the perfume compositions or an unperfumed control was applied to the axillae of the panel members in accordance with a statistical design.

After a period of five hours the axillary odour was judged by three trained female assessors who scored the odour intensity on the 0 to 5 scale, as shown below.

Score	Odour level	Conc. of aqueous isovaleric acid (ml/l)
0	No odour	0
1	Slight	0.013
2	Definite	0.053
3	Moderate	0.22
4	Strong	0.87

5	Very Strong	3.57

Average scores for each test product and the control product were then determined and the score for each test product was subtracted from the score for the control product to give the Odour Reduction Value.

Average panel score perfume A	2.08
Control panel score	2.31
Odour Reduction Value perfume A	0.23
Odour Reduction Value as percentage of control score	10%

Difference for significance @95% 0.21
Difference for significance @99% 0.28

Average panel score perfume B	1.98
Control panel score	2.31
Odour Reduction Value perfume B	0.33
Odour Reduction Value as percentage of control score	14%

Difference for significance @ 95% 0.21
Difference for significance @ 99% 0.28

Perfume A contained 47.5% and perfume B contained 54% of active perfume components.

CLAIMS

1. A cosmetic method for reducing or preventing body malodour by topically applying to human skin a composition comprising an active agent capable of inactivating body malodour-causing micro-organisms comprising corynebacteria, wherein the agent is a perfume component which is capable of inactivating the corynebacteria capable of catabolising fatty acids.

2. A method according to claim 1 wherein the composition is a perfume composition comprising at least 30% by weight of one or more of the perfume components capable of inactivating the corynebacteria capable of catabolising fatty acids.

3. A method according to either one of claims 1 and 2 wherein the perfume component comprises at least one of the following materials (Z)-3,4,5,6,6-pentamethylhept-3-en-2-one, mixtures of diethyl- and dimethyl-cyclohex-2-en-1-one, citronellol, 2-methyl-3-(4-(1-methylethyl)phenyl)propanal, (2-(methyloxy)-4-propyl-1-benzenol), diphenylmethane, tetrahydrolinalol, 4-(4-methyl-3-pentenyl)cyclohex-3-ene-1-carbaldehyde, 3-(4-methyl-3-pentenyl)cyclohex -3-ene-1-carbaldehyde, 3-(1,3-benzodioxol -5-yl)-2-methylpropanal, α-ionone, β-ionone, tricyclo[5.2.1.0,2,6]dec-4-en-8-yl ethanoate, 4-(4-hydroxy-4-methylpentyl)cyclohex -3-enecarbaldehyde, 3-(4-hydroxy-4-methylpentyl)- cyclohex-3-enecarbaldehyde, methyl iso-eugenol, 2-(1,1-dimethylethyl)cyclohexyl ethanoate, 4-(1,1-dimethylethyl)cyclohexyl ethanoate, 4-methyl-2-(2-methylprop-1-enyl)tetrahydropyran.

4. A method according to any one of the preceding claims wherein an Odour Reduction Value of at least 10% is obtained.

5. A method according to any one of the preceding claims wherein the perfume component inactivates the corynebacteria capable of catabolising fatty acids.

6. The use of a perfume component to inactivate the corynebacteria capable of catabolising fatty acids.

7. The use of a perfume composition, comprising at least 30% by weight of one or more perfume components capable of inactivating the corynebacteria capable of catabolising fatty acids, to reduce body malodour.

8. The use of a deodorant product, comprising a perfume component, to reduce body malodour by inactivating the corynebacteria capable of catabolising fatty acids.

9. A perfume composition comprising at least 30% by weight of one or more of the perfume components listed in claim 3.

10. A deodorant product comprising a perfume composition defined in claim 9.

11. A method of producing a perfume composition which comprises (i) evaluating perfume components on the ability to inhibit fatty acid metabolism in corynebacteria, (ii) selecting perfume components on the ability to sub-lethally inhibit fatty acid metabolism in corynebacteria, and (iii) mixing together two or more of said selected perfume components, optionally with other perfume components.

12. A method according to claim 11 wherein the selected perfume components are one or more of the perfume components listed in claim 3.

INTERNATIONAL SEARCH REPORT

Int tional Application No
PCT/GB 99/02165

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K7/32 A61K7/46

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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X	US 5 554 588 A (BEHAN JOHN M ET AL) 10 September 1996 (1996-09-10) abstract column 1, line 60 -column 2, line 3 examples 5-8 column 16, line 1 -column 17, line 9 claims 12,20,21	1-4,9,10

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Y		3

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

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"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
4 November 1999	16/11/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Cielen, E

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INTERNATIONAL SEARCH REPORT

Int[illegible]ional Application No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
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INTERNATIONAL SEARCH REPORT

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